(10 000/mm³) with 78% neutrophils. Plasma sodium concentration was 121 mmol(mEq)/l, and urea and potassium concentrations were normal. Serum aspartate aminotransferase activity was 180 IU/l (normal 3-35 IU/l) and serum amylase activity 390 IU/l (normal 40-160 IU/l). A chest x-ray film showed extensive consolidation in the left lung. No pathogenic organisms were isolated from sputum or blood cultures. Indirect fluorescence tests on admission and days 8, 11, and 21 showed antibody titres to *Legionella pneumophila* of 1/8, 1/32, 1/64, and 1/128 respectively. There was no serological evidence of infection with influenza, respiratory syncytial virus or adenovirus, group B chlamydia, or *Mycoplasma pneumoniae*.

As legionnaires' disease was suspected on admission he was given erythromycin 500 mg four times daily for 10 days. The abscess of the appendix was treated conservatively with intravenous fluids, and gentamicin and metronidazole were given for 10 days. On this regimen his condition improved steadily, the pneumonia having cleared clinically and radiologically after 12 days in hospital. Appendicectomy was performed two months later. Histological examination showed a subacute abscess with no specific features. He has remained asymptomatic since the operation.

Comment

Although abdominal symptoms are often present in patients with legionnaires' disease, structural lesions of the gastrointestinal tract have not been found at necropsy. The symptoms of appendicitis were this patient's main complaint—in fact, despite extensive pneumonia, he complained of a dry cough only on direct questioning. While this may have been a chance association, I believe that this complication might be overlooked in a patient severely ill with respiratory failure or encephalopathy, and if not treated correctly might have a deleterious effect on the outcome.

I thank Dr T Rowbotham for the legionella serology, Mr T Brennan for his surgical advice, and Dr J Stevenson for permission to report on this patient.

¹ Anonymous. Legionnaires' disease. *Br Med J* 1978;iii:1319-20.

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Spacing between doses on a thrice-daily regimen

The effect of drug treatment is related not only to the number of doses taken but also to the timing of doses. This is particularly true for drugs with a narrow therapeutic range and a short elimination half-life. While considerable variations in the patients' interpretations of the prescription label have been reported,¹ the spacing between doses has not been studied objectively. We used a recording medication monitor² to study the spacing between doses by patients on a thrice-daily regimen and to study the validity of interview data on the timing of doses.

Patients, methods, and results

The medication behaviour of 82 patients (45 men, 37 women) aged 56-90 years who were being treated with pilocarpine thrice daily for simple glaucoma was studied for three weeks with a medication monitor, which recorded the date and hour each time the medication bottle was opened.² Other sources of the drug were controlled, and the patients were not told that their drug-taking was being monitored until all the data had been collected.

From each monitor record we determined the three times (more than two hours apart) when doses were most frequently taken. For each patient the spacing between doses was then determined as the intervals between these times. Monitor records from five patients were lost for technical reasons. The mean of the first, second, and third intervals was 6.4, 6.5, and 11.1 hours respectively (table). The third interval was 12 hours or more for 30 (39%) patients. Only four patients took the drug at eight-hourly intervals. In the most extreme case the patient took the drug at intervals of three, three, and 18 hours. The patients studied took their drug at relatively similar intervals from day to day: 68 (88%) took at least 80% of their doses within one hour of their usual time.

After the recording period the patients were asked at which hours of the day they usually took the drug. Five patients were lost from these interviews. Comparisons with data from the monitor showed good agreement: for 85% of the intervals the difference was one hour or less. Only nine patients reported an interval with a deviation of more than two hours from that recorded by the monitor.

Comment

Although interview data on missed doses are often inaccurate,³ our findings show that interviews with patients were accurate in determining the spacing between doses. In studies of medication compliance data on the spacing between doses gained at interview may be combined with other methods to determine the number of doses taken—for example, pill count. In routine medical practice interviews may be useful for obtaining information about irregular dosage intervals and as a first step towards improving the situation.

A striking finding was the irregular timing of doses among patients on a thrice-daily regimen. Assuming that the effective duration of the drug is about eight hours,⁴ it is probable that long night intervals unfavourably influence the result of the treatment. Among patients with a twice-daily regimen Hermann found a tendency to spread doses more regularly, with an average night interval of 13.6 hours.¹ There is evidence that the proportion of missed doses is lower with a twice-daily than with a thrice-daily regimen.⁵

Hence, both in terms of missed doses and of spacing between doses, drugs prescribed twice daily will probably be more properly administered than those prescribed three times a day. When it is not possible to reduce the frequency of doses tailoring of doses to daily routines may improve compliance both in terms of spacing and of missed doses.⁵

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¹ Hermann F. The outpatient prescription label as a source of medication errors. *Am J Hosp Pharm* 1973;30:155-9.

² Norell SE, Granström P-A, Wassén R. A medication monitor and fluorescence technique designed to study medication behaviour. *Acta Ophthalmol (Copenh)* 1980;58:459-67.

³ Norell SE. Accuracy of patient interview and estimates by clinical staff in determining medication compliance. *Soc Sci Med* (in press).

⁴ Heilmann K, Richardson KT, eds. *Glaucoma: conceptions of a disease*. Stuttgart: G Thieme, 1978: 272.

⁵ Norell SE. Medication behaviour: a study of outpatients treated with pilocarpine eye drops for primary open-angle glaucoma. *Acta Ophthalmol [Suppl] (Copenh)* 1980;143.

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Intervals between doses of pilocarpine prescribed three times daily

Duration of interval (hours)	0	-1½	-2½	-3½	-4½	-5½	-6½	-7½	-8½	-9½	-10½	-11½	-12½	-13½	-14½	-15½	-16½	-17½	-18½	-20
No of patients				5	7	11	First interval			15	17	16	5	1						
No of patients				3	7	9	Second interval			19	16	16	6	1						
No of patients							Third interval			1	8	10	13	15	14	7	2	5	1	1